



Genzyme Corporation
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November 11, 2009

RE: Reports of Foreign Particles in Cerezyme[®] (imiglucerase for injection), Fabrazyme[®] (agalsidase beta), Myozyme[®] (alglucosidase alfa) and Aldurazyme[®] (laronidase)

Dear Health Care Practitioner,

Genzyme has detected foreign particles in some products filled at the Allston Landing facility in the course of routine quality control processes. Genzyme has also received customer reports of foreign particles in some vials of these products. The particles observed include non-latex rubber originating from the stopper, or stainless steel particles or fiber-like material originating from the manufacturing process. To help ensure that patients are not exposed to foreign particles during product administration, we are writing to alert health care practitioners of the potential presence of such foreign particles and reinforce recommendations consistent with the approved product labeling for product preparation and administration. These findings are unrelated to the decontamination of the Allston Landing facility.

Foreign particles identified by visual inspection prior to administration ranged in size from 120-500 microns. Genzyme recommends using a 0.2 or 0.22 micron in-line filter to prevent particulates from entering the bloodstream. Without prior filtration, intravenous injection of foreign particles of this size most likely would remain close to the injection site (Madsen R. et al). This could cause local venous damage or injection site reactions such as pain or local irritation. However, particles can theoretically migrate and cause embolic phenomena. Should this occur, the organ most likely affected would be the lung resulting in pulmonary emboli and/or foreign body granuloma and may manifest as symptoms ranging from mild respiratory discomfort to respiratory failure. In the presence of cardiac septal defects other organs could be affected.

To better understand these potential risks to patients, Genzyme has reviewed the global safety database which contains all adverse events reported to Genzyme for these products from January 2007 through 5 Nov 2009. This review has not identified any safety concerns to suggest that patients treated with Genzyme products have been exposed to foreign particles. The safety profile for these products remains unchanged.



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We are providing the following recommendations for Cerezyme, Fabrazyme, Myozyme and Aldurazyme lots filled in the Allston Landing facility and specifically identified with the prefix "A" (e.g., Lot A12345):

1. Perform a visual examination of the lyophilized product prior to reconstitution. For Aldurazyme, examine the liquid solution. **Do not use if there are foreign particles and use a new product vial.**
2. Follow the preparation instructions provided in the Dosage and Administration section of the approved product labeling.
3. As stated in the approved product labeling, visually inspect the reconstituted product within each vial and when withdrawn into the syringe and during dilution into the infusion bag for any particles. **Do not use if there are any particles and use a new product vial.**
4. If foreign particles are observed, report to Genzyme Medical Information at 800-745-4447 (option 2). Please return vials containing foreign particles per instruction to be provided by Genzyme Medical Information.
5. Aldurazyme, Cerezyme, Fabrazyme, and Myozyme should be filtered during administration of the infusion. Use an in-line, 0.2 or 0.22 micron, low protein binding filter. While it is assumed that visible particles (i.e. $> 50 \mu\text{m}$) will be retained by the recommended 0.2 or 0.22 micron filters, Genzyme has not yet performed studies to assure filter integrity is maintained on filtration of product that may contain such particles.
6. Unused vials or reconstituted product should be refrigerated within the conditions specified in the approved labeling.

Should you require further information or have any questions, please do not hesitate to contact us at 800-745-4447 (option 2). We can also be reached by email at medinfo@genzyme.com.

Yours sincerely,

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